Reactor's Comments to Papers Presented at the Herschel S. Horowitz Memorial Symposium: Recent Advances in the Fluoride Legacy

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About My Colleague Dr. Horowitz

On December 17, 2003, a memorial symposium was held at the National Institutes of Health to celebrate the science and legacy of Herschel Horowitz. For those of you interested in learning more than you hear today at this special session devoted to Hersh's contributions to dental public health, the proceedings of the symposium will appear in a special issue of the *Journal of Public Health Dentistry* (1).

There are those in any profession who are generalists who know less and less about more and more. Then there are those who are specialists (like Sherlock Holmes) who know more and more about less and less. And then there are the talented few like Hersh who combined the best of the qualities of each. He was a much sought after invited speaker and prolific writer. The National Library of Medicine electronic data base for the period 1966–2003 lists almost 150 journal publications for Horowitz HS. Consider the varying topics that Hersh wrote seminal papers on and the numerous research areas in which his expertise was widely recognized:

—community water fluoridation
—school water fluoridation
—partial defluoridation of community water supplies
—dietary fluoride supplements
—pit and fissure sealants
—professional administered fluorides
—indexes for the measurement of dental fluorosis
—self-administered fluorides (dentifrices, mouthrinses)
—prenatal effects of fluorides
—research issues in early childhood caries
—biomedical ethics
—cost-benefit analysis
—combined effects of cariostatic agents
—examiner bias
—inter- and intraexaminer variability

And I could go on and on. In terms of my own experience in working with Hersh, I believe that his overarching expertise was to help develop, improve, and make more uniform the principles for the clinical testing of cariostatic agents and take issue with irrational arguments. What can be more damaging to the advancement of medical/dental knowledge than research that fosters the use of ineffective agents or that misses the detection of potentially effective ones? Advancement in the science of conducting dental clinical trials to mitigate these problems is perhaps the most important legacy of Hersh Horowitz. Early on, the profession came to heed the prudent scientific positions in dental public health that he affirmed. Prudent because they were based on rigorous research, sound data, and warranted conclusions. Following is my own selection of some significant positions (in no particular order) that Hersh enunciated:

> (W)ater fluoridation was never intended to provide a precise dosage of fluoride (unlike dietary fluoride supplements). The selection of one part fluoride per million parts of water was selected as a target concentration for community water fluoridation because, from extensive epidemiologic surveys, it was learned that it was a compromise concentration that would provide maximal prevention of dental caries with a minimal prevention prevalence of dental fluorosis. (2)

> Because the morbidity of dental caries has declined undue emphasis has been placed on the risks of using fluoride rather than on its profound beneficial effects. The emphasis may have become overblown and may ignore the past seriousness of dental caries as a disease over apprehension of dental fluorosis, a cosmetic condition. (2)

> For groups without access to other sources of fluoride having high risk of dental caries, water fluoridation remains as effective as it ever was. The diffusion effects of fluoridated water and dilution effect from other sources of fluoride primarily explain the decline in benefits between F and non-F communities. (3)

> It is inconceivable to suggest that systemic methods of fluoride not be implemented or discontinued because young children can be exposed to various dosages of topical fluoride products that should not be ingested. (4)

> Early use of fluoride toothpastes in young children clearly has been implicated as a risk factor for dental fluorosis. This risk greatly outweighs the few percentage points that may be lost by these children using lower potency toothpastes than the 1000 to 1500 ppm F concentrations currently marketed. (2)

> Because caries risk assessment is such an imprecise science and impractical and complex to interpret and implement, it is unlikely that the practitioner can ascertain who is at high risk. (5)

[Hersh questioned CDC's recommendation that fluoride supplements be judiciously prescribed for high-risk children and supported the 1994 ADA conservative revised dosage schedule

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for children who consume water with insufficient concentrations of fluoride.]

I believe Hersh would like most to be remembered for his research contributions that helped to improve the dental health of the public. The ongoing efforts of our profession to prevent dental disease are greatly diminished by his loss.

Reaction to Featherstone's, Newbrun's, and Estupiñán-Day's Papers

There are abundant human epidemiologic data to show that water fluoridation provides a substantial topical effect in preventing dental caries in teeth already erupted when first exposed to fluoridated water (6,7). Clinical data thus are highly correlated with in vitro and in situ experimental models of fluoride-hydroxyapatite systems, which show that slightly elevated, low concentrations of fluoride in saliva and plaque fluid decrease the rate of enamel demineralization and enhance the rate of remineralization (8). One might wonder why this type of mechanism action of fluoride had not been widely recognized sooner, for Torrell and Ericsson back in 1965 in a multigroup clinical trial showed that daily rinsing with a low potency 0.05 percent sodium fluoride solution produced significantly greater caries protection than other groups receiving various professional and self-applied topical fluoride procedures including a group rinsing fortnightly with a more concentrated 0.2 percent sodium fluoride solution (9).

For many years the prevailing view of most scientists was that the anticaries activity of fluoride was principally a result of its preeruptive effect on developing enamel to make it more resistant to acid dissolution (10,11).This theory that preeruptive incorporation of fluoride in enamel as the sole mechanism of action is no longer widely believed (12). Data from numerous studies of water fluoridation and other systemic fluoride methods support the view of both a preeruptive (systemic) effect and a posteruptive (topical) effect (13). In more recent reviews of the clinical evidence of fluorides preeruptive and posteruptive effects, Murray concluded that at 15 years of age the maximum DMFS reduction in a fluoridated area was about half to preeruptive and half to posteruptive (14). Beltrán and Burt concluded that both preeruptive and posteruptive exposure are operative in the anticaries effect, with current research giving posteruptive effect the greater influence (6). Similarly, CDC's evaluation of the evidence of how fluoride prevents dental caries indicates that it works primarily posteruptively (7).

Some scientists now have gone further and largely discounted a preeruptive effect of fluoride (15,16). However, clinical evidence to support this major shift in how fluoride works is limited and, at best, dubious. In the longitudinal study by Hardwick and coworkers, the primary aim was to determine whether there was a posteruptive effect on children who were 12 years of age at the start of water fluoridation (17). Results after 4 years showed a significant 25 percent reduction, which mainly was derived from teeth present at the baseline, proving the authors hypothesis. Results for the much fewer teeth that erupted during the study showed a similar caries reduction in terms of attack rate of surfaces at risk. However, you can hardly negate a preeruptive effect on unerupted teeth in children who are first exposed to fluoridated water at age 12 years.

Also in the epidemiologic study by Stamm and co-workers showing the effectiveness of fluoridated water on root caries in adults, the participants were lifelong residents of Stratford, a natural fluoride community (18). Therefore, both pre- and posteruptive exposure could have contributed to the effect.

The literature contains many epidemiologic studies that support the value of a preeruptive effect of systemic fluoride ingestion (4,6,13). Although it is difficult to separate out preeruptive from posteruptive effects, the early Tiel-Culemborg (19) and the recent Australian studies (20) cited by Newbrun were perhaps the most thoroughly analyzed to answer this question. Burt has described the Tiel-Culemborg study as "rigorously controlled, more so than the original four North American studies" (21). The Australian study used individual histories of fluoride exposure relative to age of eruption of the first permanent molars and controlled for a host of potential confounding variables. Findings of the study are in agreement with the earlier Tiel-Culemborg study in demonstrating anticaries effectiveness of preeruptive exposure to fluoridated water. The multiple linear regression showed a decreasing caries experience with increasing preeruptive fluoride exposure Also in agreement with the Tiel-Culemborg study were the bivariate results segregated by type of surface showing a greater effect on pit and fissure surfaces compared with the other types of surfaces. However, there are several negative aspects of the study that limit its value as supporting evidence. The study failed to detect a significant caries preventive effect from posteruptive exposure alone, yet there is no discussion nor explanation offered for this contradictory finding. Next, the model R-squared showed that less than 12 percent of the variance in first molar DMFS scores could be explained by all the independent variables, an indication that the model did not fit the data too well. Lastly, because of the exceedingly large sample sizes a mean difference of as small as 0.16 DMFS proved highly significant (P=.000). Notwithstanding, when you look at all the clinical data, the weight of the evidence supports the importance of exposure to both preeruptive effect from birth and continuous posteruptive effect throughout life to water fluoridation in order to provide maximum anticaries protection to the deciduous and permanent dentitions.

Considering the difficulties involved in clinically differentiating a preeruptive from a posteruptive effect compared with the relative ease in demonstrating only a posteruptive effect, I can only echo Dr. Newbrun's cautionary statement that, regardless of findings of laboratory models or animal experiments, the proof of a theorized "minimal" preeruptive effect must come from human clinical studies.

Commenting on Estupiñán-Day's paper, one can only be impressed with the rate of progress PAHO has made in bringing the benefits of salt fluoridation to the people of Central and South America. Its cariostatic effectiveness over an extended period of time appears to be comparable to that of water fluoridation. But quoting Dr. Dario Restrepo of the World Health Organization,

The dental profession must not

consider salt fluoridation a substitute for water fluoridation for the prevention of dental caries. It is an alternate method of preventing dental decay to be employed in areas where fluoridation is urgently needed, but because of inadequate water systems these areas are unable to benefit from water treatment procedures (22).

In Europe, both fluoridated and unfluoridated salt is available and the ministries of health make little effort in promoting fluoridated salt. PAHOs approach has been to work with governments to institute national programs of salt fluoridation in which all people benefit as with water fluoridation. According to Marthaler (23), compared with Europe, PAHO has been successful in this approach because dental caries is much higher in Latin America and there is a greater need for mass methods of caries prevention; many Latin American ministries have staff with formal training in public health, whereas in Europe postgraduate training in this specialty is not widespread; and antifluoridation movements are much stronger in Europe and in most cases are supported by the media.

DMFT results of the five countries with consolidated salt fluoridation programs shown in Estupiñán-Day's paper indicate substantial reductions in dental caries, varying from 42 to 84 percent, and all have met WHO's objective for the year 2000 of three or fewer DMFT (24). (Incidentally, in the United States 1986–87 national survey, 12-year-old children had 1.79 DMFT) (25). In these types of before-and-after cross-sectional studies it is difficult to control for secular trends and the many variables that can influence dental caries. For example, in a detailed report of the Jamaica program (26), the first national salt program to be implemented in the Americas, fluoride toothpaste had been introduced 15 years prior to the introduction of salt fluoridation in 1987 and data on its use were not collected on the baseline or in 1995. The report, however, discusses several limitations of the study and the authors acknowledge that the observed change in caries prevalence between the two surveys can be attributed to a combination of factors. However, they indicate that because fluoridated salt was the dominant factor of change during the period of study, it was the most likely factor to have contributed to the decreased caries prevalence. Further, the findings are in accord with results of other of PAHO's salt fluoridation programs in the Americas (26) and with reports from several European countries where the benefits of fluoridated salt have been demonstrated consistently (26,27).

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